UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,587	12/04/2001	Michael A. Tainsky	0788.00063	5172

48924 7590 04/01/2008

KOHN & ASSOCIATES, PLLC
30500 NORTHWESTERN HWY
STE 410
FARMINGTON HILLS, MI 48334

EXAMINER	
CLOW, LORI A	

ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
04/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/004,587	TAINSKY ET AL.	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9 January 2008 has been entered.

Applicants' response, filed 8 February January 2008, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim 20 is currently pending. Claims 1-19 have been cancelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejections herein are either re-iterated or newly applied based on claim amendments.

Claim 20 recites, "obtaining epitope bearing clones displaying reactivity to antibodies present in sera of patients with early stage cancer but not in sera of normal individuals" and "identifying all epitope bearing clones that are specific to early stage cancer as markers

indicative of early stage cancer". As step one only obtains sera from normal individuals and patients with cancer (not any specific stage of cancer) it remains unclear as to what is indicative of early stage cancer. Clarification is requested.

Claim 20, as amended, recites, "identifying all epitope bearing clones that are specific to early stage cancer as markers indicative of early stage cancer". It is unclear as to how a clone can be a marker. The epitope itself can be a marker. Clarification is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claim 20, as amended, recites, "identifying all epitope bearing clones that are specific to early stage cancer as markers indicative of early stage cancer". Applicant has not provided support, nor is support apparent for such a limitation that a "clone" is a "marker". The Specification teaches that "the term "marker" as used herein is intended to include, but is not limited to, a gene or a piece of a gene which codes for a protein, a protein such as a fusion protein, open reading frames such as ESTs, **epitopes**, mimitopes, and any other indicator of

immune response. A combination of markers, or an array, is used in order to better analyze the sera of the patient. This array or combination is at least two markers which can be used to diagnose or stage a disease (page 17, lines 7-13)". The Specification further teaches that "in order to develop an effective screening test for early detection of ovarian cancer, cDNA phage display libraries are used to **isolate cDNAs coding for epitopes** reacting with antibodies present specifically in the sera of patients with ovarian cancer (page 25, lines 5-8)".

Therefore, the Specification provides support for an epitope itself to be a marker but not for a clone to be a marker, as is instantly claimed. As such, the claim contains NEW MATTER.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

I.

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sioud et al. (European Journal of Immunology (2001) Vol. 31, pages 716-725; previously cited) in view of WO 99/39210 (5 August 1999; Miller et al; previously cited). This rejection is re-instated from the Office Action of 2 March 2007 as necessitated by amendment to the claim which now recites "microarray".

The instant claims are drawn to a method of detecting and identifying markers indicative of early stage cancer by differentially biopanning sera from normal and cancer patients and obtaining epitope bearing clones present in the disease stage based upon antibody reactivity, identifying epitope bearing clones as markers of early stage cancer and including those in a microarray.

Sioud teaches the analysis of the humoral response in patients with cancer. Libraries from breast cancer cell lines were biopanned and positive clones were selected. Using serum antibodies from patients with breast cancer, IgG-binding phage-encoded cDNA products were

selected and the clones identified important antigens including p53, pentraxin and others. The selected phage-displayed cDNA products were recognized by a significant number of breast cancer sera as compared to normal individuals (abstract; Results and Discussion section 2.2 on page 717).

Sioud et al. do not specifically teach a "microarray" of markers within sera. However, Miller et al. teach a high-density protein array for proteome analysis (page 1, lines 5-21). The array may be for high throughput and can be constructed on microtitre wells, membrane support, silicon chips or grids (page 17, lines 1-13).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have utilized the techniques of Sioud to biopan and select clones to array in a large format, as presented by Miller. One would have been motivated to do so because Miller teaches that primary arrays may be developed to emulate antigenic diversity of a cell, tissue, organ, organism from which a biological sample is derived (page 5, lines 16-19). The arrays may be used for comparative purposes to determine whether the protein profile of a "test sample" possess any differences in terms of expressed proteins to a biological reference (page 6, lines 15-16). Miller teaches the use of the arrays to diagnose a human or animal for a medical condition, ailment, illness, or immune response by comparing proteins detected in the biological sample with proteins in a standard, wherein the differences are indicative of the medical condition, ailment, illness, or immune response (page 11, lines 16-30).

II.

Claims 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sioud et al. (European Journal of Immunology (2001) Vol. 31, pages 716-725; recited previously), in view of 2003/0003516 (2 January 2003 with priority to 10 April 2001; Robinson et al.).

The instant claims are drawn to a method of detecting and identifying markers indicative of early stage cancer by differentially biopanning sera from normal and cancer patients and obtaining epitope bearing clones present in the disease stage based upon antibody reactivity, identifying epitope bearing clones as markers of early stage cancer and including those in a microarray.

Sioud teaches the analysis of the humoral response in patients with cancer. Libraries from breast cancer cell lines were biopanned and positive clones were selected. Using serum antibodies from patients with breast cancer, IgG-binding phage-encoded cDNA products were selected and the clones identified important antigens including p53, pentraxin and others. The selected phage-displayed cDNA products were recognized by a significant number of breast cancer sera as compared to normal individuals (abstract; Results and Discussion section 2.2 on page 717).

Sioud et al. do not specifically teach a "microarray" of markers within sera. However, Robinson et al. teach an epitope array for determining a specificity profile in a patient (page 2, paragraph 0009). The arrays are high density (page 2, paragraph 0016).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have used the methods of Sioud with the high-density arrays of Robinson. One

would have been motivated to do so because Robinson teaches the use of arrays or epitopes, for example, to screen for disease (page 6, paragraph 0047).

Response to Applicant's Arguments with regard to Sioud et al.

1. Applicant argues that "there is no disclosure or suggestion in the Sioud et al. reference of a method or assay that simultaneously screens for unlimited number of markers within sera".

This argument is moot in view of the newly applied reference under 35 USC 103 above. Further, the instant claim does not include limitations to "unlimited number of markers" or to "simultaneous screening". Finally, Sioud et al. teach the identification of markers in patients with cancer versus normal individuals. Sioud et al. identify more than one marker from biopanned sera. Sioud et al. identify all epitopes that were identified in cancer versus non-cancer individuals. See page 718, for example, which states:

Positive phage clones are clearly distinguishable from negative clones, confirming the specificity of the immunoreaction. To evaluate the presence or absence of antibodies against the selected phage-encoded cDNA products in normal and cancer patient sera, phage particles from random individual positive clones were purified and tested by an immunospot assay (Fig. 3) as a representative example. The immunoreactivity was quantitated with densitometric imaging using ImageQuant software. Most phages showed a strong reactivity with patient IgG as compared to the reactivity obtained with normal IgG.

2. Applicant argues that the methodology of Sioud et al. "teaches away from the use of a large array, or more specifically including all epitopes uncovers during biopanning related to a disease because in the first full paragraph of Sioud et al. reference is to….enrich for the best binders".

This is not persuasive. As was previously stated, the claimed method, now directed to a microarray, is taught by the combination of Sioud and Miller or Sioud and Robinson. Further,

while Sioud teaches the enrichment for the best binders, the teaching does not preclude finding multiple markers, as is instantly claimed.

3. Applicant argues that the "present invention provides "unexpected results" by providing a broad range, yet sensitive assay capable of detecting early stage cancer". Applicant asserts that "the prior art does not provide markers nor does it even suggest the provision of markers for such early-stage detection of cancer".

This is not persuasive. The presentation of a broad range yet sensitive assay for detection of cancer is not proof of unexpected results. Sioud teach a biopanning method and phage selection for normal versus cancer patients, thus teaching the same "assay" that Applicant argues is "unexpected".

Further, Applicant is reminded that evidence relied upon should establish "that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance." Ex parte Gelles, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992) and that the arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965).

Conclusion

Claim 20 is not allowed.

The outstanding rejections under 35 USC 102(b) have been withdrawn in view of the claim amendments. Newly applied rejections under 35 USC 103 are now pending.

Applicants arguments with regard to Sioud as a 102 reference have been considered and are persuasive in terms of Sioud not teaching a "microarray".

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

/Lori A. Clow, Ph.D./

Primary Examiner, Art Unit 1631